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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,780	07/22/2002	Christopher John Secombes	ABLE-0021	9521
26259	7590	11/29/2004	EXAMINER	
LICATLA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053			KELLY, ROBERT M	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 11/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/088,780	Applicant(s) SECOMBES ET AL.	
	Examiner Robert M Kelly	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7,9-18,21-26,28-40 and 42-54 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7,9-18,21-26,28-40 and 42-54 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 September 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>9/16/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendments and arguments of 16 September 2004 have been entered.

Claims 8, 27 and 41 have been cancelled.

Claims 1, 14, 21, 33, 38, and 50 have been amended.

Claims 1-7, 9-18, 21-26, 28-40, and 42-54 are presently pending and considered.

Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

In light of Applicant's amendments and arguments of 16 September 2004, the objection to the specification for not complying with sequence requirements, is withdrawn.

Priority

In light of Applicant's amendments and arguments of 16 September 2004, the objection to the specification for lacking a claim to priority, is withdrawn.

Drawings

In light of Applicant's amendments and arguments of 16 September 2004, the objection to drawing 1 for not containing a proper label, is withdrawn.

Claim Objections

In light of Applicant's cancellation of Claim 41 and arguments of 16 September 2004, the objection to Claim 41 is moot, and thus withdrawn.

Claim Rejections - 35 USC § 112 – second paragraph, old rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In light of Applicant's cancellation of Claim 41 and arguments of 16 September 2004, the rejection of Claim 41, for being indefinite, is moot, and thus withdrawn.

Claims 14, 33, and 38 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Response to Arguments 35 USC 112 – second paragraph, old rejections

Applicant's arguments of 16 September 2004 have been fully considered but are not persuasive.

Applicant argues that by amending the claims to recite "two amino acid substitutions in the H-chain respectively" is sufficient to overcome the indefinite nature of the claims (Applicant's response of 16 September 2004, p. 15, paragraph 2). Such is not persuasive because meaning of the term "respectively" is still unclear. Applicant has failed to address this part of the quoted limitation.

Claim Rejections - 35 USC § 112, second paragraph – Necessitated by Amendment

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 9-18, 21-26, 28-37, 44-45, 47-48, and 51-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and

distinctly claim the subject matter which applicant regards as the invention, for reasons necessitated by the amendments.

Independent Claims 1 and 21 each recite the limitation "... a non-infection nucleic acid which upon administration to the animal encodes a recombinant antibody ...". It is unclear how such nucleic acid could only encode the antibody upon administration. Moreover, it is unclear if it encodes the antibody during the process of administering the nucleic acid, or if it encodes the antibody after administration.

Claims 2-7, 9-18, 22-26, 28-37, 44-45, 47-48, and 51-53 are rejected for depending from Claims 1 or 21 and not further clarifying the indefinite nature of the independent claim from which it depends.

Claim Rejections - 35 USC § 112, first paragraph – old rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of Applicant's cancellation of Claims 8, 27 and 4, the rejection of those claims under 35 USC 112, first paragraph, are moot, and thus are withdrawn.

Claims 1-7, 9-18, 21-26, 28-40, and 42-54 remain rejected under 35 U.S.C. 112, first paragraph, for reasons record in the Official Action of 6 April 2004, pp. 5-19, because the specification, while being enabling for a composition for protection of a fish against viral haemorrhagic septicaemia virus (VHSV) comprising a non-infectious DNA nucleic acid construct encoding the single chain antibody 3F1H10 that recognizes VHSV, the DNA sequence

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for the antibody listed on pages 9-10 of the specification and which comprises substitutions of asparagines 35a with threonine and lysine 64 with threonine and is linked at the 5' end to the secretion signal of transforming growth factor beta, and which sequences is operably linked to the CMV promoter and a polyA tail for protecting a fish against VHSV infection, and vaccines comprising such compositions, and methods of providing prophylactic treatment of fish against VHSV by the administration of these compositions, by injection into the epaxial muscles below the dorsal fin, which compositions transform cells of the muscle tissue local to the injection site and produce secreted 3F1H10 antibodies, thereby producing protection against VHSV, does not reasonably provide enablement for any nucleic acid construct encoding any antibody, any secretion sequence, any promoter sequence, any form of administration, any form of composition, treatment of any animal, or any form of treatment for any disease-causing agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Response to Arguments – 35 USC § 112, first paragraph – old rejection

Applicant's arguments of 16 September 2004 have been fully considered but are not persuasive.

Applicant argues that the Examiner has incorrectly characterized the claims, as being drawn to any nucleic acid construct encoding any antibody, but should be characterized as any non-infectious nucleic acid construct encoding any recombinant antibody against any disease-causing agent (Applicant's response of 16 September 2004, p. 17, paragraph 3).

Such is not considered persuasive. The breadth of the claims given consideration is generally summed up by the statement on page 10, last paragraph, of the Official Action of 6 April 2004, wherein it is stated: "Because these claims are broad, encompassing compositions and the use of such compositions for treating any animal for any disease-causing agent by the administration of a wide range of nucleic acids encoding any antibody or antibodies, without limitation to forms of administration or regulatory constructs, the detail of the disclosure provided by Applicant, in view of the prior art, must encompass a wide area of knowledge, to a reasonably comprehensive extent." Clearly, from this statement and the claims, the Examiner considered only non-infectious nucleic acid constructs and antibodies. The reason that such antibodies is not limited to "antibodies against a disease causing agent" is that such antibody may have been raised against another non-disease causing agent, yet still recognize the disease causing agent, and the claims are not limited to "antibodies raised against a disease-causing agent in a [pick your animal] and that recognize the disease-causing agent".

Applicant argues that by providing a list of possible pathogens (pp. 5-6 of the specification), exemplary signal sequences (pp. 6-7 of the specification), and various routes of delivery (p. 7), that the broad aspects of the invention are, in fact enabled (Applicant's response of 16 September 2004, pp. 17-18, paragraph bridging).

Such is not considered persuasive. Applicant's listing of theoretical pathogens, signal sequences, and routes of delivery, do not overcome the enablement for reasons of record in the Official Action of 6 April 2004. Specifically, with regard to Applicant's disclosure in the specification:

However, such broad discussion does not constitute the specific guidance and direction that would allow the Artisan to predict that any specific recombinant

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antibody, any form of nucleic acid, any disease-causing agent, any animal, any regulatory sequences, or any form of administration could be used for treatment of any specific condition. The Artisan could not reasonably predict, as reviewed in the nature of the invention and state of the prior art, that enough nucleic acid would reach the target tissue, transform the target tissue, produce enough stable and functional mRNA, and proteins therefrom, and the protein would be stable and functional, and processed correctly, to produce enough of an effect, for a long enough period of time to effect any specific treatment, and, moreover, that CTL responses would not nullify any such effects.

(Official Action of 6 April 2004, p. 16, paragraph 2). Moreover, Applicant has not provided any reasoning to overcome these issues.

Applicant asserts, using a co-submitted Declaration by Mr. Niels Lorensen, that the Artisan could make and use other nucleic acid constructs other than the exemplary 3F1H10 antibody encoding construct that recognizes VHSV in fish (Applicant's response of 16 September 2004). The declaration of Mr. Lorensen declares that a similar construct encoding a single-chain antibody to a toxin was prepared and tested in mice (Declaration of Mr. Lorensen, paragraph 2). Mr. Lorensen further declares that the antibody gene was inserted downstream of the CMV promoter in a plasmid that was delivered to mice by intramuscular injection, followed by electroporation, and a delay or inhibition of toxic effects of the toxin was observed when the mice were later exposed to the toxin (Id.).

Such is not persuasive. First, it is pointed out that the method of administration is not limited to intramuscular injection, followed by electroporation, in the claims. Second, it is unknown what toxin, what antibody construct, or what epitope(s) of the toxin were recognized. Third it is not known whether a delay or inhibition of toxic effects were observed, and how much toxin was added, and how it compares to the administration of toxins without prior antibody administration. Fourth, even if this second embodiment is fully enabled for that specific mode of administration, form of vector, toxin, and animal, etc., it is simply enabling for that; and even

when it is considered with the 3F1H10 antibody in fish, such is not found to enable the full scope of the claims because, for any particular embodiment:

Such experimentation would be required to determine which forms of nucleic acid could be used, which agents could be treated, which animals could be treated, which form of administration could be used, which types of treatment could be effected, which secretion sequences to use, whether to use a secretion sequence, whether multiple genes could be used, which promoters would be required, which immune system deficiencies could be treated, if any, and whether such treatments would produce enough transformed cells that produce enough stable and functional mRNA and proteins therefrom, for a long enough period of time to effect treatment.

(Official Action of 6 April 2004, p. 18, paragraph 3).

Applicant cites *In re Skrivan*, 427 F.2d 801, 806, 166 USPQ 85, 88 (CCPA 1970) for the statement “We hold that claims need not recite such factors where one of ordinary skill in the art, to whom the specification and claims are directed, would consider them obvious” (*Id.*), to assert that the compositions, promoter signals, routes of administration, formulations, which are asserted to be well known and obvious, need not be specifically recited in the claims (Applicant’s response of 16 September 2004, pp. 18-19, paragraph bridging).

Such is not considered persuasive. First, the holding was emphasized to deal with only “a physical operating condition of an admittedly old process” (*Skrivan* at 88), and further deals with “Jepson” claims (*Id.*). It is clear that the holding, because it deals with Jepson claims, which are improvements over old processes, already known in the art, and because the holding emphasizes the import of the process being “admittedly old”, this holding is not binding on this instant case, which is not an old, well-known, process, but instead to asserted novel compositions and methods (e.g., Specification at p. 3, paragraph 4). Moreover, regardless of such holding, claims are still required to be enabled for their full breadth when a method is involved or an intended use is stated (MPEP 2164.08 [R-1]).

Applicant argues that MPEP 2164.08, *W.L. Gore & Assoc., Inc.*, and *In re Johnson*, that the specification is looked to for how to practice the invention, not the claims, and therefore, the suggestions to include claim limitations limited to the 3F1H10 antibody and fish are clearly related to practice of the invention, and should not be outlined in the claims (Applicant's arguments of 16 September 2004, p. 19, paragraph 2).

Such is not considered persuasive. With regard to *W.L. Gore & Assoc., Inc.*, the holding with regard to enablement was concerned with the fact that a particular term, "stretch rate", may not have been enabled, but it was found enabled because (1) no evidence of record existed to rebut the enablement of the claims; and (2) there was uncontradicted evidence of record that "stretch rate" had a particular meaning known to those of skill in the art at the time of filing of the Application. Hence, this holding does not apply to the present case, where it would have required undue experimentation to work out any particular embodiment (Official Action of 6 April 2004, p. 18, paragraphs 2-3). With regard to *In re Johnson*, the holding hinged on the fact that, "The PTO would limit appellants to claims reciting a sigma σ value of at least 0.7. This view is improper because it requires the claims to set forth the practical limits of operation for the invention and it effectively ignores the scope of enablement provided by the specification as a whole." (*Johnson* at 195). *Johnson* is distinguished from the present case because the claims are not enabled for their full scope for reasons of record in the Official Action of 6 April 2004, pp. 5-19). Moreover, the same holdings, and the MPEP at 2164.08 requires that the claims be enabled for their full scope. For reasons which Applicant has failed to rebut so far, the Claims are not enabled for their fully-claimed scope (*Id.*).

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The Applicant further supports their previous argument by citing *In re Goffe* to state that it would not serve the constitutional purpose of promoting progress in the sciences to limit Applicants to their disclosed embodiments or preferred materials (Applicant's arguments of 16 September 2004, pp. 19-20, paragraphs bridging).

Such is not considered persuasive. While it is agreed that it would not serve the purpose of promoting progress in sciences to limit the Applicant thusly, it is further asserted that the claims must be enabled for their fully claimed scope (MPEP 2164). While these two arguments may seem to conflict in certain cases, as in the instant case, they do not. In fact, in many arts, for example the mechanical arts, the art is very predictable, e.g., what is encompassed by a bottle-cap would be made as easily as it is envisioned; hence, a Claim to a bottle-cap would not require the specification to disclose type of bottle-cap. However, in the instant case, an insufficient number of embodiments exist, and the art is not sufficiently predictable; therefore, the scope of enablement is proper. For any particular embodiment in the present case, the Artisan would be required to perform laborious experimentation to determine whether:

Such experimentation would be required to determine which forms of nucleic acid could be used, which agents could be treated, which animals could be treated, which form of administration could be used, which types of treatment could be effected, which secretion sequences to use, whether to use a secretion sequence, whether multiple genes could be used, which promoters would be required, which immune system deficiencies could be treated, if any, and whether such treatments would produce enough transformed cells that produce enough stable and functional mRNA and proteins therefrom, for a long enough period of time to effect treatment.

(Official Action of 6 April 2004, p. 18, paragraph 3).

Because of the breadth of the claims, the following rejections

are held, even in light of the scope of enablement.

Claim Rejections - 35 USC § 102 – old rejections, Duan

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In light of Applicant's amendments, cancellations, and arguments of 16 September 2004, the rejection of Claims 1-7, 9, 12-13, 16-18, 21-27, 31-32, 35-37, and 44-54 under 35 U.S.C. 102(b) as being anticipated by WIPO Doc. No.: WO 96/37234 to Duan, et al., Filed 23 May 1996, Published 28 November 1996, are either mooted and/or withdrawn.

Claim Rejections - 35 USC § 102 – old rejections, Chang

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In light of Applicant's cancellation of Claims 8 and 27 in the response of 16 April 2004, the rejection of these claims under 35 USC 102 by Chang is moot, and therefore withdrawn.

Claims 1, 15, 21, and 34 remain rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,543,144 to Chang, filed 21 January 1993; date of patent 6 August 1996.

It is noted that Applicant has incorporated the limitations of the cancelled claims (a secretion sequence) into independent claims 1 and 21, and limited the intended use of the compositions to encoding the antibodies after administration to an animal.

Response to Arguments - 35 USC § 102 – old rejections, Chang

Applicant's arguments of 16 September 2004 have been fully considered but are not persuasive.

Applicant argues that Chang teaches administering the nucleic acids to cells, from which the antibodies are collected and administered to patients, and hence the limitations of the claims are not taught. Applicant also asserts that the limitation that the antibody is not encoded until after administration to an animal is also not taught by Chang. (Applicant's arguments of 16 September 2004, pp. 21-22).

Such is not persuasive. Intended use is not considered limiting in art rejections for composition claims: the composition is the composition (MPEP 2111.02 [R-2]). Moreover, because of the indefinite nature of Applicant's claim (See pages 3-4 of this Official Action), the rejection is maintained, as it meets all the other aspects of the claims.

Claim Rejections - 35 USC § 103 – Necessitated by the Amendments

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7, 9, 12-13, 16-18, 21-27, 31-32, 35-37, 44-48, and 50-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over WIPO Doc. No.: WO 96/37234 to Duan, et al., Filed 23 May 1996, Published 28 November 1996.

Those aspects taught by Duan are discussed below, with respect to each, followed by a listing of what is not taught, what is obvious, and why, and then a statement with regard to obviousness given.

With regard to Claims 1, 7, 21, 44, and 48, Duan teaches gene therapy by administering a gene that encodes an antibody that binds an antigen associated with a disease (disease causing agent) (ABSTRACT; p. 22, lines 12-29). Moreover, Duan teaches that such administered compositions preferably are in the form of non-cytopathic eukaryotic viruses (non-infectious nucleic acids) (p. 17, lines 18-22). Furthermore, the antibody may comprise variable heavy and light chains, joined by a linker (p. 14, lines 19-32).

With regard to Claims 2, 22, and 51-53, Duan teaches treating fish and mammals and humans (p. 10, lines 14-17).

With regard to Claim 3, 23, and 46, because Duan teaches treating diseases after such diseases have taken effect, as well as treating HIV infection, (p. 4, lines 6-18), and because the major effect of HIV is immune system deficiency, Duan inherently teaches use in animals with deficient immune systems.

With regard to Claim 4, 24 and 45, the disease causing-agent may be a pathogen, e.g., viruses (p. 2, line 3-p. 3, line 23).

With regard to Claim 5 and 25, the compositions may be administered prophylactically (p. 20, lines 7-13).

With regard to Claim 6, 26, and 47, the antibody may be derived from an antibody raised against the disease-causing agent (p. 14, lines 19-32).

With regard to Claim 9 and 28, Duan teaches that multiple antibodies to different epitopes may be used (p. 22, line 30-p. 23, line 9).

With regard to Claim 12 and 31, Duan teaches a virus-neutralizing antibody (EXAMPLE 23).

With regard to Claim 13 and 32, the antibody is a single-chain molecule (EXAMPLE 23).

With regard to Claim 16 and 35, Duan teaches a DNA form of vector (p. 43, lines 5-8).

With regard to Claim 17 and 36, Duan teaches intravenous, perfusion, and topical treatment (p. 17, lines 15-18), which encompasses at least liquids, ointments, and paints.

With regard to Claim 18 and 37, Duan teaches intravenous, perfusion, and topical treatment (p. 17, lines 15-18), which encompasses at least injection.

With regard to Claim 50, Duan teaches gene therapy by administering a gene that encodes an antibody that binds an antigen associated with a disease (disease causing agent) (ABSTRACT; p. 22, lines 12-29). Moreover, Duan teaches that such administered compositions preferably are in the form of non-cytopathic eukaryotic viruses (non-infectious nucleic acids) (p. 17, lines 18-22). Furthermore, Duan teaches that multiple antibodies to different epitopes may be used (p. 22, line 30-p. 23, line 9), and because Duan teaches treating diseases after such diseases have taken effect, as well as treating HIV infection, (p. 4, lines 6-18), and because the major effect of HIV is immune system deficiency, Duan inherently teaches use in animals with deficient immune systems.

With regard to Claim 54, Duan teaches treating humans (p. 10, lines 14-17).

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However, Duan does not teach the use of secretion sequences, stating:

Because intracellular expression is desired, the recombinant genes of the invention preferably are prepared so as to be free of a signal sequence. "Free of a signal sequence" means a deletion, mutation or modification of the signal sequence which ordinarily directs antibodies to the secretory compartments. For example, the hydrophobic amino acid core of the signal sequence for secretion can be substituted with hydrophilic residues by site directed mutagenesis. See Biocca, S. et al., "Expression and Targeting of Intracellular Antibodies in Mammalian cells," European Molecular Biology Organization (EMBO) Journal 1: 101 (1990).

(Id., p. 14, paragraph 2)

Hence, at the time of invention by Applicant, it would have been obvious to one of skill in the art to modify the compositions and methods of Duan to include the signal sequence of the antibody within the nucleic acids, and to administer such compositions to patients. The Artisan would have been motivated to do so in order to obtain extracellular expression and protect against extracellular pathogens. Moreover, the Artisan would have had a reasonable expectation of success because these antibodies naturally included such signal sequences, and Duan was removing them in order stop secretion (Id.).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M Kelly whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PRIMARY EXAMINER

